Eperythrozoon suis infections in pigs: Clinical syndromes and diagnosis

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Summary: *Eperythrozoon suis is a bacterial organism that infects red blood cells of pigs. Infected pigs may die from severe anemia, or they may become chronically infected and develop a variety of clinical syndromes including decreased weight gain, failure to thrive, reproductive failures, and increased susceptibility to respiratory or enteric bacterial infections. No FDA-approved drugs are available to treat infected pigs. Presently, E. suis infection is diagnosed by identifying the organisms in blood smears or by serological testing for antibodies produced during infection. Both of these methods have severe limitations because of variability of parasitemia and antibody production. A method to diagnose eperythrozoonosis by directly detecting E. suis DNA in blood samples using the polymerase chain reaction is under development.*

Eperythrozoon suis is a rickettsial bacterium that infects red blood cells of pigs. *Eperythrozoon suis* adheres to the outer membrane of red blood cells , deforming and damaging them. In this location, *E. suis* uses plasma glucose for its own metabolism. Damaged red blood cells are subsequently removed from the circulation or may undergo intravascular lysis, resulting in anemia and icterus in acutely ill animals. Death usually results from anemia or hypoglycemia. Chronically infected pigs have suppressed T-lymphocyte function, which increases their susceptibility to other diseases.

At present, there are no FDA-approved drugs for the treatment of *E. suis* infection in swine. Tetracyclines or arsenicals eliminate signs of acute illness and prevent death, but these compounds do not clear the animal of infection. Treated animals become chronic carriers and may serve as sources of infection for the rest of the herd through transmission of blood or plasma by lice, mosquitoes, or contaminated needles.

The prevalence of *E. suis* infection and its impact on the swine industry is not fully known and is somewhat controversial. Various serologic surveys using the indirect hemagglutination assay (IHA) in the South and Midwest indicate that 16%– 40% of tested herds had animals with positive antibody titers. While direct losses due to acute eperythrozoonosis have declined, indirect losses from chronically infected animals (reproductive losses, feed-efficiency losses) continue to occur and are difficult to fully measure.

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Diagnostic notes are not peer-reviewed.

Clinical syndromes

Eperythrozoon suis infection has two distinct clinical manifestations:

- acute "icteroanemia" in growing pigs; and
- chronic eperythrozoonosis, which is often subclinical and can occur at any level of production.

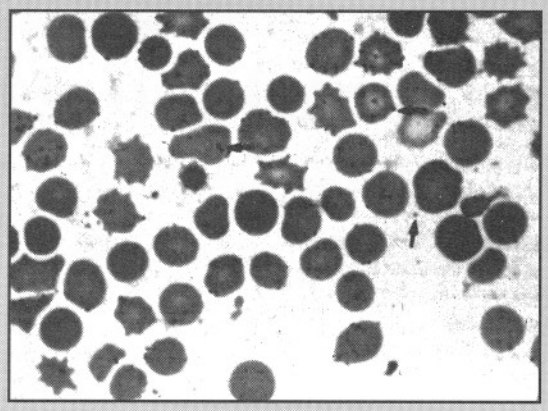
The incidence of acute eperythrozoonosis has decreased since the disease was first characterized in the 1930s. This is thought to be due to the use of feed additives containing arsenicals and to improved ectoparasite control, although acute icteroanemia is still occasionally seen in feeder pigs during times of stress (shipping, high environmental temperature, etc.). As the use of feed additives becomes further restricted, it is possible that acute icteroanemia could increase in prevalence.

Pigs acutely ill with eperythrozoonosis are anorectic, lethargic, and febrile. Icterus and anemia develop shortly after the onset of clinical signs. Some pigs develop subcutaneous edema, necrosis of the extremities of the ears, or become more likely to bleed. Left untreated, the disease progresses rapidly with death occurring 1–5 days after the onset of clinical signs. Mortality in pigs showing clinical signs is high. On postmortem, the blood is thin and exhibits spontaneous agglutination. Carcasses are often pale and severely icteric. Some animals have ascites, hydrothorax, and hydropericardium.

Chronic *E. suis* infections are associated with several discrete syndromes in pigs during various stages of production. These include:

- increased susceptibility to enteric and respiratory bacterial infections;
- failure to thrive, debilitation, and decreased tolerance for "stress;"
- chronic, low-grade (often subclinical) anemias;
- reproductive failures, cycling irregularities, and decreased conception rates in sows and gilts; and
- decreased birth weights, anemia in neonatal pigs,. and increased numbers of stillborn pigs.

Figure 1



Giemsa-stained blood smear showing *Eperythrozoon suis* organizisms on red blood cells and free in the plasma (arrows). Approximately 80% of the cells have one or more *E. suis* organisms, and infected cells show moderate to marked deformation. When less that 50% of red cells are parasitized, the diagnosis is often overlooked. Original magnification: ×1000.

Chronically infected animals may have recrudescence of parasitemia during times of stress (shipping, breeding, lactation, etc.), often accompanied by fever and anorexia. During these times, spread of infection to susceptible pigs may occur via biting insects or contaminated needles. Necropsy findings in chronically infected animals are generally non-specific and may relate to general debilitation or secondary bacterial infections.

Diagnosis

Diagnosis of acute eperythrozoonosis is based on history, clinical signs, necropsy findings, and identifying the organisms on Wright's stained blood smears (e.g. Diff-Quik™), where *E. suis* appears as 0.5–1.0 mm, coccoid, rod- or ring-shaped basophilic particles on red blood cells or free in the plasma (Figure 1). *Eperythrozoon suis* organisms may be arranged in linear chains on the erythrocyte membrane. During episodes of intense parasitemia, the organisms may circumscribe the entire red blood cell. Parasitemia declines rapidly as parasitized cells are removed from the blood, often before the animal has shown significant clinical signs. For this reason, blood smears from anemic pigs may contain few *E. suis* organisms, and the diagnosis of eperythrozoonosis may be overlooked. The organisms are frequently confused with artifacts of light microscopy, further impeding microscopic identification. *Eperythrozoon suis* organisms are nonrefractile, of fairly consistent size, and often distort the shape of the red blood cell.

Diagnosis of chronically infected pigs is difficult because parasitemia in these animals is sporadic and frequently missed. Herds with chronically infected individuals typically have increased incidence of respiratory and enteric diseases, and this occurs in spite of good management practices. Conception rates are often lower than expected, and estrus cycles may be irregular. Baby pigs (infected in utero) are often smaller than normal; these pigs often develop icterus and anemia at 7–10 days of age which, while infrequently fatal, often results in stunting and failure to thrive. Occasionally, a growing pig may suddenly die with anemia and icterus. Attempts to identify *E. suis* organisms in the blood of these animals is often difficult. Definitive diagnosis in herds such as this may be aided by serological tests.

Serological tests such as the IHA measure IgM antibodies produced during *E. suis* infection. The IgM antibodies are targeted toward the damaged RBC membrane, not the *E. suis* organism itself. Once damaged RBCs have been removed from circulation, IgM levels rapidly decline and become undetectable. Antibody production varies considerably among individual pigs. Young pigs (<3 months of age) have very poor antibody responses to *E. suis* infection. IgM levels are more frequently detected in sows than in boars or growing pigs, probably because parasitemia periodically recrudesces during lactation and breeding, stimulating antibody production.

Because antibody production in infected pigs is highly variable and unreliable, false-negative IHA titers can occur with great frequency. For this reason, the IHA is useful for screening herds, but is of less value in detecting infection in individual animals. A reliable test is needed to accurately detect *E. suis* infected pigs, which would allow elimination of infected animals from a herd.

Two new assays are in development (but are not yet currently available) that may enhance our ability to detect chronically infected pigs. The first of these is an enzyme-linked immunosorbent assay (ELISA) that has increased sensitivity when compared to the IHA. Unfortunately, this test still shares the pitfalls of the IHA in that it relies on measurement of IgM antibody levels, which are highly variable among infected animals.

The second of these assays weds molecular biology with disease diagnosis. This procedure uses the polymerase chain reaction (PCR) to directly amplify DNA from *E. suis* in an infected blood sample. The PCR technique has several advantages over antibody-driven serological techniques including increased sensitivity and the ability to directly detect *E. suis* DNA in a blood sample. Currently this test is under development in order to adapt it to a diagnostic laboratory setting. Advantages of this test include:

- ability to identify chronically infected carriers to eliminate them from the herd; and
- prepurchase screening to prevent introducing infected animals into a herd.

Eperythrozoon suis infection in pigs can result in significant losses within a herd, both as a primary pathogen and as a contributor to other disease states. Eperythrozoonosis is often suspected in herds with health problems that persist in spite of intensive therapeutic and management changes.

Currently, accurate diagnosis is frequently difficult due to the inability to reliably detect infection in acutely and chronically infected animals. With the development of a reliable test to detect chronic *E. suis* infection, steps can be made toward adequate

control of infection within and between herds. Additionally, reliable testing would allow epidemiologic data to be gathered and the true impact of *E. suis* infection on the swine industry to be determined.

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